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FDA Summary

Novoste Beta-Cath System
Novoste Corporation
P000018

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FDA Summary

- FDA Review Team
- Device Description
- Nonclinical Evaluation
- Clinical Evaluation
- Panel Questions

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FDA Review Team

- ODE - K. Peters
R. Subramanian
B. Zuckerman
- OST - T. Heaton
- OSB - G. Kamer
- OC - M. Linde

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Device Description

- β -Cath™ Delivery Catheter
- Transfer Device
- Source Train
- System Accessories

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Device Description (cont.)

- Alpha III and Alpha IV Transfer Device Models used in Clinical Evaluation
- Alpha IV Rev. 2 Transfer Device Subject of PMA
- Optional Accessories

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Device Description (cont.)

- 30mm and 40mm Delivery Catheters and Source Trains used in Clinical Evaluation
- Source Trains Differ by the Number of Seeds (12 vs. 16)
- Only 30mm Delivery Catheter and Source Train Subject of PMA

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Nonclinical Evaluation

- *In Vitro* Testing
- Biocompatibility Testing
- Electrical, Battery, & EMC Testing
- *In Vivo* (Animal) Testing
- Source Dosimetry

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Clinical Investigations

- Beta Energy Restenosis Trial (BERT)
 - US Feasibility Investigation (de novo)
- Beta Radiation in Europe Trial (Brie)
 - Registry (de novo)
- Stents and Radiation Therapy Trial (START)
 - Randomized (in-stent restenosis)

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Clinical Evaluation

Bram Zuckerman, MD

Medical Officer, DCRD

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START Trial

- Prospective, multicenter, triple-masked RCT
- 476 patients with in-stent restenosis
- Randomized to beta source or placebo

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START Trial

- Symptomatic target lesion in native coronary vessels between 2.7 and 4.0 mm in diameter
- Lesion was suitable for treatment with a 30- or 40- mm clinical source train after treatment with 20- or 30-mm balloon respectively
- Radiation dose determined by visual estimate of vessel size

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START Trial

- Superiority Hypothesis
- Primary study endpoint was Target Vessel Failure (TVF) at 8 months
 - TVF = composite of Death, MI, TVR
- Angiographic and ultrasound data are supporting data

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Acute Results

	SR-90	PLACEBO	95% CI of Difference	P-VALUE
DEVICE SUCCESS	98.4%	97.8%	(-1.9,3.0%)	0.680
PROCEDURE SUCCESS	97.1%	97.0%	(-2.9,3.2%)	0.924
POST-PROCEDURE STENT SEGMENT PERCENT DIAMETER STENOSIS	22.9 ±13.5%	22.9% ±12.9%	(-2.4,2.4)	0.997

Acute Device Performance

- Device Failure (unsuccessful delivery of Beta-Cath System) - 1.9% (9/476)
 - Catheter not successfully delivered - 1.3% (6/476)
 - Source not successfully delivered - 0.6% (3/476)

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Acute Device Performance (Cont.)

- Initial Device Failure with subsequent success - 2.1%(10/476)
- "Minor" Device Malfunction 18.7%(89/476)
 - system used successfully but performance was suboptimal
- Bail-out Box used - 1.3% (6/476)
- NRC or State Reports - N = 1

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8 Month Results - Safety

	SR-90	PLACEBO	95% CI OF DIFFERENCE
Death	1.2%	0.4%	(-0.8, 2.4%)
Myocardial Infarction	1.6%	3.0%	(-4.1, 1.3%)
Stent Thrombosis (< 30 days)	0.0%	0.4%	(-1.3, 0.4%)
Site Thrombosis (Days 31 - 240)	0.0%	0.0%	-----
Total Occlusions	4.0%	3.7%	(-3.5, 4.2%)
Aneurysm	0.5%	0.0%	(-0.5, 1.5%)

* One Site Thrombosis event occurred at 244 days in SR-90 arm

8 Month Results - Effectiveness

	SR-90	PLACEBO	95% CI OF DIFFERENCE	P- VALUE
TVF-FREE AT 240 DAYS	81.4%	72.2%	(0.3, 18.1%)	0.0393
TVR-FREE AT 240 DAYS	83.5%	73.8%	(1.1, 18.3%)	0.0283
8 MONTH ANALYSIS SEGMENT BINARY RESTENOSIS RATE	28.8%	45.2%	(-25.9, -6.9%)	0.0008
8 MONTH STENT SEGMENT BINARY RESTENOSIS RATE	14.2%	41.2%	(-35.5, -18.4%)	0.0001

Conclusions

The primary endpoint, TVF, as well as selected clinical and angiographic endpoints were all reduced by beta radiation treatment

No difference in incidence of death, MI, stent thrombosis, or total occlusion

Device-related malfunctions were observed

Panel Questions

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Panel Question 1

1. Please discuss your recommendations for the antiplatelet therapy for patients who receive a new stent, and for patients who do not receive a new stent.

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Panel Question 2

2. Please discuss the clinical importance of the device failure and malfunction events in the evaluation of the safety and effectiveness of the Beta-Cath System.

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Panel Question 3

3. Please discuss whether you believe the probable clinical benefit of the radiation treatment outweighs the probable risks of death, myocardial infarction, late total occlusion, and late stent thrombosis posed by the device in the intended patient population.

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Panel Question 4

- 4a. Please comment on the indications for use section (page 12) as to whether it identifies the appropriate patient population for treatment with the device.
- 4b. Please comment on the contraindications section (page 12) as to whether it identifies all conditions under which the device should not be used because the risk of use clearly outweighs any possible benefit.

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Panel Question 4 (cont.)

- 4c. Please comment on the warnings and precautions sections as to whether it identifies all potential hazards regarding device use.
- 4d. Please discuss whether any improvements could be made to the labeling to help minimize the occurrence of device failures and malfunctions as discussed under question 2.

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Panel Question 4 (cont.)

4e. Please comment on the remainder of the device labeling as to whether it adequately describes how the device should be used to maximize benefits and minimize adverse events.

4f. Does the panel have any other recommendations regarding the labeling of the device?

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Panel Question 5

5a. Please discuss any improvements that could be made to the training program to help minimize the occurrence of device failures and malfunctions as discussed under question 2.

5b. Please identify any other important elements that should be contained in a physicians training program for this device.

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Panel Question 6

6. Based on the clinical data provided in the panel pack, do you believe that additional clinical follow-up data or post-market studies are necessary to evaluate the chronic effects of intravascular radiation administration? If so, how long should patients be followed, and what endpoints and adverse events should be measured?

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